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Tonix Pharmaceuticals Announces Peer-Reviewed Publication in mSphere Journal Highlighting the Tolerability of Company's Single-Dose Mpox and Smallpox Vaccine Candidate TNX-801, in Immune-Compromised Animals

The World Health Organization (WHO) declared the spread of new Clade Ib Mpox a public health emergency of international concern (PHEIC): Second Mpox-related WHO PHEIC declaration in two years

Clade Ib Mpox cases detected in 16 African countries and outside of Africa, in Sweden, Thailand, Singapore, India, Germany and England

Single-dose mpox vaccines with durable protection may be required to address global health emergency

TNX-801 was shown to be more than 10- to 1,000-fold more attenuated (or less virulent) compared to the older vaccinia smallpox vaccines: Tolerability of TNX-801 vaccination in immune-compromised animal models supports clinical development

CHATHAM, N.J., Nov. 13, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, today announced the publication of a paper entitled, "*Recombinant Chimeric Horsepox Virus (TNX-801) is Attenuated Relative to Vaccinia Virus Strains in Both In Vitro and In Vivo Models*," in the peer-reviewed journal *mSphere*. The publication presents data demonstrating that TNX-801 is less virulent than 20th Century vaccinia vaccines in immune-compromised mice. Previously, single-dose vaccination with TNX-801 was shown to protect animals from a lethal challenge with Clade Ia monkeypox.

On August 14, 2024, WHO determined that the upsurge of Clade Ib mpox in Africa constituted a public health emergency of international concern (PHEIC), the second such declaration in the past two years in response to an mpox outbreak. The recent ongoing outbreak is caused by Clade Ib monkeypox virus, while the PHEIC declared in 2022, and still ongoing, is caused by Clade IIb monkeypox virus. Mpox cases of the new clade Ib monkeypox virus have been detect in 16 African countries and Sweden, Thailand, Singapore, India, Germany and England. The new Clade Ib mpox is spreading in children in Africa and so far, has been carried by adult travellers from Africa into non-African countries.

The global mpox outbreak from Clade IIb, which commenced in 2022, has affected over 90,000 people in countries where mpox had previously not been endemic, including Europe and the U.S. The Clade IIb mpox from the 2022 PHEIC predominantly affects gay men outside of Africa and already is an established endemic in the U.S.

“Addressing the new Clade Ib mpox outbreak and the ongoing spread of Clade IIb mpox may require a single dose mpox vaccine that provides durable protection,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “TNX-801 previously has demonstrated the ability to protect animals from lethal challenge with Clade Ia monkeypox virus. The new findings reported in the peer-reviewed journal *mSphere* show tolerability of TNX-801 in immune-compromised animals which further supports testing in humans. In addition, we expect TNX-801 can be distributed and stored without a costly supply chain.”

The publication describes data in which TNX-801 was compared with older vaccinia vaccine strains used in the eradication of smallpox for tolerability in both *in vitro* and *in vivo* models. Together, TNX-801 was shown to be more than 10- to 1,000-fold more attenuated (or less virulent) compared to the older vaccinia smallpox vaccines. Combined with the ability of TNX-801 to protect animals against lethal challenge with Clade Ia monkeypox virus, the Company believes that the new tolerability data support the idea that TNX-801 is a candidate vaccine to control the ongoing PHEICs with mpox Clade Ib and mpox Clade IIb.

About TNX-801*

TNX-801 (recombinant horsepox virus) is a minimally replicating, live virus vaccine based on horsepox in pre-clinical development to prevent mpox and smallpox. Tonix reported positive preclinical efficacy data, demonstrating that TNX-801 vaccination protected non-human primates against lethal challenge with monkeypox.[1] After a single dose vaccination, TNX-801 prevented clinical disease and lesions and also decreased shedding in the mouth and lungs of non-human primates.[1] The findings are consistent with mucosal immunity and suggest the ability to block forward transmission, similar to Dr. Edward Jenner’s vaccine, which eradicated smallpox and kept mpox out of the human population.[1] TNX-801 is based on synthesized horsepox which is believed to be more closely related to Dr. Jenner’s vaccine than 20th Century vaccinia viruses.[2] Smallpox vaccines, descended from Jenner’s vaccine, used prior to 1900 would be called horsepox by modern nomenclature.[3-5] TNX-801 is delivered percutaneously with only one dose and therefore may achieve higher rates of community protection than two-dose vaccines by eliminating drop-out between doses and limiting forward transmission. Tonix has received official written response from a Type B pre-Investigational New Drug Application (IND) meeting with the U.S. Food and Drug Administration (FDA) to develop TNX-801 as a potential vaccine to protect against mpox disease and smallpox.[3] Tonix announced a collaboration to develop GMP manufacturing processes for its mpox vaccine with Bilthoven Biologics (Bbio), part of the world’s largest vaccine manufacturer, the Cyrus Poonawalla Group, which also includes the Serum Institute of India. Tonix also announced a collaboration with the Kenya Medical Research Institute (KEMRI) to design, plan and seek regulatory approval for a Phase I clinical study of TNX-801 in Kenya. The Company believes TNX-801 has the potential to make a global impact on mpox and the risk of smallpox because of its durable T-cell immune response, the potential to manufacture at scale, and the use of a lower dose than non-replicating vaccines. The FDA-approved non-replicating mpox vaccine Jynneos® requires two doses and provides a

relatively short duration of protection.[7,8] FDA also recently approved ACAM2000, a live, replicating vaccinia vaccine for prevention of mpox.[9] ACAM200 is a clone from DryVax®, a 20th Century vaccinia vaccine derived from the NYCBH strain. Pre-clinical results from an mRNA vaccine recently showed some protection from a Clade I monkeypox challenge, but with multiple break-through lesions in vaccinated animals.[10]

About the Recombinant Pox Vaccine (RPV) Vaccine Platform*

On the horsepox platform, Tonix is developing TNX-1800 (horsepox expressing SARS-CoV-2 spike protein) for protecting against COVID-19. TNX-1800 is an engineered version of horsepox that expresses the spike protein of SARS-CoV-2. In preclinical studies of TNX-1800 highlighted in the presentation, TNX-1800 was tested for immunogenicity and efficacy of TNX-1800 in nonhuman primates following a SARS CoV-2 challenge.[11,12] TNX-1800 vaccination results in a neutralizing antibody response that was associated with significant reduction in virus replication/shedding in the respiratory tract and tolerability.[11,12] TNX-1800 was selected by the NIH's, Project NextGen for inclusion in clinical trials as part of a select group of next generation COVID-19 vaccine candidates with the intent to identify promising vaccine platforms. NIH plans to conduct a Phase 1 trial of TNX-1800 and cover the full cost of the study, while Tonix provides the vaccine candidate.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully integrated biopharmaceutical company focused on transforming therapies for pain management and vaccines for public health challenges. Our priority is to advance our TNX-102 SL product candidate for the management of fibromyalgia, for which a New Drug Application ("NDA") was submitted to the U.S. Food and Drug Administration ("FDA") in October 2024, based on two statistically significant Phase 3 studies. The FDA granted Fast Track designation to TNX-102 SL for the management of fibromyalgia in the third quarter. We expect an FDA decision on the acceptance of the NDA for review and PDUFA date in December and if accepted, a decision on NDA approval in 2025. Fibromyalgia is a common chronic pain condition that affect mostly women. Fibromyalgia is now recognized as the prototypic nociplastic pain syndrome. TNX-102 SL is a non-opioid, centrally acting analgesic developed for long-term use in fibromyalgia. If approved, TNX-102 SL would be the first new drug therapy for fibromyalgia in more than 15 years. TNX-102 SL is also being developed to treat acute stress reaction and acute stress disorder under a Physician-Initiated Investigational New Drug application ("IND") at the University of North Carolina in the OASIS study funded by the U.S. Department of Defense (DoD). We expect to initiate enrollment in the OASIS study in the fourth quarter. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic drug candidate in Phase 2 development designed to treat cocaine intoxication that has FDA Breakthrough Therapy designation and its development is supported by a grant from the U.S. National Institute of Drug Abuse and Addiction. Our immunology development portfolio includes TNX-1500, which is an Fc-modified humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) in Phase 1 development for the prevention of allograft rejection and for the treatment of autoimmune diseases. TNX-1700 is a fusion protein of TFF2 and albumin and is in the pre-IND stage of development to treat gastric and pancreatic cancer. Tonix also has pre-clinical product candidates in development in the areas of rare disease, including TNX-2900 for Prader-Willi syndrome, and infectious disease, including TNX-801 a potential vaccine to prevent mpox and

smallpox. Tonix recently announced a contract with the U.S. DoD's Defense Threat Reduction Agency ("DTRA") for up to $34 million over five years to develop TNX-4200, small molecule broad-spectrum antiviral agents targeting CD45 for the prevention or treatment of infections to improve the medical readiness of military personnel in biological threat environments. Tonix owns and operates a state-of-the art infectious disease research facility in Frederick, MD. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

* Tonix's product development candidates are investigational new drugs or biologics; their efficacy and safety have not been established and have not been approved for any indication.

Zembrace SymTouch and Tosymra are registered trademarks of Tonix Medicines. All other marks are property of their respective owners.

(1) Noyce RS, et al. *Viruses*. 2023;15(2):356. https://doi.org/10.3390/v15020356
(2) Noyce RS, et al. *PLoS One.* 2018 Jan 19;13(1):e0188453. doi: 10.1371/journal.pone.0188453. PMID: 29351298; PMCID: PMC5774680.
(3) Schrick L, et al. *N Engl J Med.* 2017;377(15):1491-1492
(4) Duggan AT, et al. Genome Biol. 2020;21(1):175.
(5) Brinkmann A, et al. Genome Biol. 2020;21(1):286.
(6) TNX-801 PR pre-IND meeting 8/20/23: https://ir.tonixpharma.com/news-events/press-releases/detail/1417/tonix-pharmaceuticals-announces-results-of-pre-ind-meeting
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(8) JAMA Collier AY, et al. *JAMA.* 2024 doi: 10.1001/jama.2024.20951. Epub ahead of print. PMID: 39361499. https://pubmed.ncbi.nlm.nih.gov/39361499/
(9) FDA Roundup August 30, 2024. www.fda.gov/news-events/press-announcements/fda-roundup-august-30-2024
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(11) Awasthi M, et al. *Viruses*. 2023 Oct 21;15(10):2131. doi: 10.3390/v15102131. PMID: 37896908; PMCID: PMC10612059.
(12) Awasthi M et al *Vaccines* (Basel). 2023 Nov 2;11(11):1682. doi: 10.3390/vaccines11111682.PMID: 38006014

This press release and further information about Tonix can be found at www.tonixpharma.com.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as "anticipate," "believe," "forecast," "estimate," "expect,"

and “intend,” among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the failure to successfully market any of our products; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission (the “SEC”) on April 1, 2024, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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